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Application No.	Ref.	Date
98 918 196.1 - 2404	P021826EP	24.04.2008
Applicant Arena Pharmaceuticals, Inc.		

Communication under Rule 71(3) EPC

You are informed that the Examining Division intends to grant a European patent on the basis of the above application with the text and drawings as indicated below:

In the text for the Contracting States:
AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

Description, Pages

1-62, 64, 66-78, 80-88	as published
65	filed with telefax on 23.11.2005
63, 79	filed with telefax on 06.02.2008

Claims, Numbers

1-19	filed with telefax on 06.02.2008

Drawings, Sheets

1/17-17/17	as published

Comments
Art 84 EPC - Description has been adapted to the new set of claims (pages 24, 50 and 51) and figure 1 has been replaced by figure 2 and vice-versa (pages 4 and 24).

In the text for the Contracting States:
AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

With the following amendments to the above-mentioned documents by the examining division

Description, Pages 4,24,50,51

A copy of the relevant documents is enclosed

The title of the invention in the three official languages of the European Patent Office, the international patent classification, the designated Contracting States, the registered name of the applicant and the bibliographic data are shown on the attached EPO Form 2056.

You are requested within a non-extendable period of **four months** of notification of this communication

1. to file 1 set of translations of the claim(s) in the two other EPO official languages;

		EUR
2a.	to pay the fee for grant including the fee for printing up to and including 35 pages; Reference 007	790.00
2b.	to pay the printing fee for the 36th and each subsequent page; number of pages: 73 Reference 008	876.00
3.	to pay the additional claim fee(s) (R. 71(6) EPC); number of claims fees payable: 0 Reference 016	0.00
	Total amount	1666.00

The mention of the grant of the patent shall be published in the European Patent Bulletin as soon as possible after the requirements concerning the translation of the claims and the payment of the fees for grant and printing, claims fees, designation fees and renewal fees as laid down in Rule 71(3), (4), (6) and (8) and (9) EPC are fulfilled.

Any divisional applications relating to this European patent application must be filed directly at the European Patent Office in Munich, The Hague or Berlin in accordance with Article 76(1) and Rule 36 EPC **before** the date on which the European Patent Bulletin mentions the grant of the patent (see Art. 97(3) EPC and OJ EPO 2/2002, 112).

If you do not approve the text intended for grant but wish to request amendments or corrections, the procedure described in Rule 71(4) EPC is to be followed.

If this communication is based upon an auxiliary request, and you reply within the time limit set that you maintain the main or a higher ranking request which is not allowable, the application will be refused (Art. 97(2) EPC).

If the enclosed claims contain amendments proposed by the Examining Division, and you reply within the time limit set that you cannot accept these amendments, refusal of the application under Article 97(2) EPC will result if agreement cannot be reached on the text for grant.

In all cases except those of the previous two paragraphs, if the fees for grant and printing or claims fees are not paid, or the translations are not filed, in due time, the European patent application will be deemed to be withdrawn (R. 71(7) EPC).

For all payments you are requested to use EPO Form 1010 or EPO Form 1010E or to refer to the relevant reference number.

After publication, the European patent specification can be downloaded free of charge from the EPO publication server https://publications.european-patent-office.org (OJ EPO 2005, 126).

Upon request in writing each proprietor will receive the certificate for the European patent **together with one copy** of the patent specification provided that the request is filed within the time limit of Rule 71(3) EPC. If such request has been previously filed, it has to be confirmed within the time limit of Rule 71(3) EPC. The requested copy is free of charge. If the request is filed after expiry of the Rule 71(3) EPC time limit, the certificate will be delivered without a copy of the patent specification.

Note on payment of renewal fees

If a renewal fee falls due between notification of the present communication and the proposed date of publication of the mention of the grant of the European patent, publication will be effected only after the renewal fee and any additional fee have been paid (R. 71(9) EPC).

Under Article 86(2) EPC, the obligation to pay renewal fees to the European Patent Office terminates with the payment of the renewal fee due in respect of the year in which the mention of the grant of the European patent is published.

Filing of translations in the Contracting States

Pursuant to Article 65(1) EPC the following Contracting States require a translation of the specification of the European patent in their/one of their official language(s) (R. 71(10) EPC), **if** this specification is not published in their/one of their official language(s)

- within **three months** of the publication of the mention of the grant:

AT	AUSTRIA	FR	FRANCE
BE	BELGIUM	GB	UNITED KINGDOM
CH	SWITZERLAND / LIECHTENSTEIN	GR	GREECE
CY	CYPRUS	IT	ITALY
DE	GERMANY	NL	NETHERLANDS
DK	DENMARK	PT	PORTUGAL
ES	SPAIN	SE	SWEDEN
FI	FINLAND		

- within **six months** of publication of the mention of the grant:

IE IRELAND

The date on which the mention of the grant of the European patent will be published in the European Patent Bulletin will be indicated in the decision to grant the European patent (EPO Form 2006A).

The translation must be filed with the national Patent Offices of the Contracting or Extension States in accordance with the provisions applying thereto in the State concerned. Further details (e.g. appointment of a national representative or indication of an address for service within the country) are given in the

EPO information brochure "National law relating to the EPC" and in the supplementary information updates published in the Official Journal of the EPO, or are available on the EPO website.

Failure to supply such translation to the Contracting or Extension States in time and in accordance with the aforementioned requirements may result in the patent being deemed to be void ab initio in the State concerned.

Important note to users of the automatic debiting procedure

The fees for grant and printing and also any additional claims fees due under Rule 71(6) EPC will be debited automatically on the date of filing of the translation of the (relevant) claims, or on the last day of the period of this communication. However, if the designation fees become due as set out in Rule 71(8) EPC and/or a renewal fee becomes due as set out in Rule 71(9) EPC, these should be paid separately by another permitted means of payment in order not to delay the publication of the mention of grant. The same applies in these circumstances to the payment of extension fees. For further details see the Arrangements for the automatic debiting procedure (AAD) and accompanying Information from the EPO concerning the automatic debiting procedure (Annexes A.1 and A.2 to the Arrangements for deposit accounts (ADA) in Supplement to OJ EPO 10/2007).

Examining Division:

Chairman:	Hinchliffe, Philippe
2nd Examiner:	Weijland, Albert
1st Examiner:	Pinheiro Vieira, E

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Enclosure(s): Form 2056
108 Copies of the relevant documents

+++ ATTENTION +++

New amounts of procedural fees as from 01.04.2008 (see OJ EPO 1/2008)!

If additional claims fees (R. 71(6) EPC)* are to be paid and payment is received on or after 01.04.2008, claims fees are only payable from the sixteenth claim onwards. New

amount to be paid: EUR 200,- per additional claim.
* to be amended

Claims:

1. An in vitro method for directly identifying a candidate compound as a compound that stimulates an ~~inverse agonist, a partial agonist, or an agonist to a~~ orphan G-protein-coupled receptor, or a compound which acts to diminish the active state of the orphan G-protein-coupled receptor, wherein the orphan G protein-coupled receptor comprises a mutation in its amino acid sequence so as to render it ~~receptor is~~ a non-endogenous constitutively activated orphan G protein-coupled receptor, said method comprising the steps of

   (a) contacting said candidate compound with said non-endogenous constitutively activated orphan G protein-coupled receptor, wherein said orphan G protein-coupled receptor is expressed on a mammalian cell; and

   (b) determining, by measurement of the ability of the compound to inhibit or stimulate receptor functionality, wherein said candidate compound is a compound that stimulates said orphan G protein-coupled receptor~~n inverse agonist, a partial agonist, an agonist~~ or a compound which acts to diminish the active state of said orphan G protein-coupled receptor.

2. The method of claim 1 wherein said mutation includes single amino acid mutations.

3. The method of claim 1 wherein said mutation is produced by using a mutational cassette.

~~4.~~ The method of claim 1 wherein the compound is determined to be an inverse agonist to said receptor.

~~3. The method of claim 1 wherein the orphan receptor is a G protein coupled cell surface orphan receptor.~~

~~4~~5. The method of claim ~~3~~1 wherein the third intracellular loop of said orphan G protein-coupled receptor comprises the following sequences: X1BBHyX2 wherein X1 is an amino acid; B is a basic amino acid; Hy is a hydrophobic amino acid, and X2 is an amino acid.

~~5~~6. The method of claim 45 wherein X1 is glycine.

~~6~~7. The method of clam 45 wherein X1 is alanine.

~~7~~8. The method of claim 45 wherein X1 is lysine.

~~8~~9. The method of claim 45 wherein Hy is alanine

~~9~~10. The method of claim 45 wherein X2 is lysine

~~10~~11. The method of claim 45 wherein X2 is arginine.

~~11~~12. The method of claim 45 wherein X2 is glutamic acid

~~12~~13. The method of claim ~~3~~1 wherein the second intracellular loop of said orphan G protein-coupled receptor comprises the following sequences: XRY wherein X can be any amino acid other than D.

~~13~~14. The method of claim 45 wherein said sequence X1BBHyX2 is an endogenous sequence.

~~14~~15. The method of claim 45 wherein said sequence X1BBHyX2 is a non-endogenous sequence.

~~15~~16. The method of claim ~~12~~13 wherein the sequence XRY is an endogenous sequence.

~~16~~17. The method of claim ~~12~~13 wherein the sequence XRY is a non-endogenous sequence.

~~17~~18. A method according to any one of the preceding claims wherein the ability of the compound to inhibit or stimulate receptor functionality is detected by measuring the change in cAMP levels when said candidate compound is contacted with said constitutively activated orphan G protein-coupled receptor.

~~18~~19. A method according to any one of the preceding claims wherein the ability of the compound to inhibit or stimulate receptor functionality is detected by measurement of [^{35}S]GTPγS binding.

~~19. A method according to claim 1 further comprising the step of formulating the compound into a pharmaceutical composition.~~